REMARKS

Applicants have cancelled claims 2, 9, 14, 16 and 17 without prejudice expressly reserving the right to pursue the subject matter of the cancelled claims in one or more subsequent application.

Applicants have amended claim 1 to recite a "sterilized" pharmaceutical composition. Support for this amendment is found e.g., on page 8, last full paragraph of the original specification. Applicants have also amended claim 1 to recite the compounds listed in Table 1, page 13, i.e. R = C_1-C_6 or cyclohexyl.

Applicants have amended claim 3 to be an independent. Support for this amended claim is found in originally filed claim 1 and differs from amended claim 1 in that it does not recite R = methyl- or ethyl and does not recite "sterilized" compositions.

Applicants have amended claim 10 such that it does not depend on now cancelled claim 9.

Claim 13 has been amended to be independent.

Applicants have amended claim 15, to depend on claim 13 rather than cancelled claim 14 and recites that the pharmaceutical preparation comprises a therapeutically effective amount of Bis(O-cyclohexyl-dithiocarbonato)palladium (II). Support for amended claim 15 is found, e.g., in Example 5.

Claims 9 and 14 stand rejected under 35 U.S.C. §112, first paragraph for purportedly being non-enabled. Although Applicants disagree Applicants have cancelled claim 9 and 14 without prejudice and thus the rejection is moot.

Claim 10 stands rejected under 35 U.S.C. §112, second paragraph for purportedly being indefinite. In view of the amendment to claim 10 to recite "A method for the treatment of a cancerous disease..." which provides antecedent

basis for the second recitation of "cancerous disease" in the claim, Applicants request that the Examiner reconsider and withdraw the rejection.

Claims 1-4, 7, 12, 16 and 17 stand rejected under 35 U.S.C. §102 for purportedly being anticipated by Watt et al. In view of the amendments to the claims and the following remarks Applicants request that the Examiner reconsider and withdraw the rejection of the claims. Applicants disagree.

Claim 1 has been amended to recite a "sterilized" pharmaceutical composition and to recite to the compounds listed in Table 1, page 13 "wherein R is methyl, ethyl, isopropyl, butyl, 2-methyl-butyl, hexyl or cyclohexyl. Watt does not disclose such sterilized compositions. Therefore, claim 1 as amended and the claims that depend on claim 1 are novel over Watt.

Watt et al. disclose Bis(ethylxanthato)palladium(II) and Bis(methylxanthato)-palladium(II): Amended claim 3 does not claim a methyl-palladium-xanthate or ethyl-palladium-xanthate. Therefore, claim 3 is also not anticipated by Watt.

In view of the amendment to the claims and the foregoing remarks Applicants request that the Examiner reconsider and withdraw the rejection of the claims.

Claims 5, 6, 9, 10, and 13-15 stand rejected under 35 U.S.C. §103(a) for purportedly being unpatentable over Watt et al in view of Amtmann et al. and further in view of Das et al. In summary, the Examiner contends that Das teaches that palladium chelates are likely to be effective anti-tumor agents and, therefore, Das would provide a general motivation for replacing the platinum with palladium in the complexes of Amtmann et al. Applicants disagree.

> "[A] proper analysis under §103 requires, inter alia, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the

> art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. . . .Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure."
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> In re Vaeck, 20 USPQ2d 1438, 1442 (CAFC 1991)

> The cited art must be considered for all that it teaches and the Examiner is not permitted to pick and choose from those teachings only so much that would render the claims obvious.
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> ATD Corp. v. Lydall, Inc. 48 USPQ2d 1321 (Fed. Cir. 1998).

The claims as amended recite particular $Pd(S_2COR)_2$ compounds, wherein R is C_1-C_6 or cyclohexyl. Applicants demonstrate in Example 2 and Table 1 of the specification that the claimed compounds surprisingly have a several fold higher cytotoxic activity on human tumor cells than the corresponding thioplatin compounds. Such an increase could not have been expected from the prior art.

Furthermore, Table 1 demonstrates that the claimed compounds have a pronounced higher cytotoxic activity at a slightly acidic pH than in the alkaline range. Such an acidic pH is found in the tissue of solid tumors and, therefore, the claimed compounds are particularly advantageous for the treatment of solid tumors. Moreover, it is supposed that drugs with such a pH dependent activity have an improved therapeutic index (see Friebolin et al., abstract., previously submitted with Applicants' Reply filed February 21, 2008). Such a pronounced cytotoxic effect at pH 6.8 of the particular compounds as recited in amended claim 1 was not suggested and could not be derived from the combined teaching of Watt et al., Amtmann et al. and Das et al.

Das et al. report that "some" transition metal chelates of Schiff bases containing N and S donor atoms posses cytotoxic activity against blood tumor cells (leukaemia), i.e. not solid tumors. Das et al. further teach that slight modifications in the structure of the ligand influence the cytotoxic activity of the metal chelates. Among the 11 palladium chelates screened only 4 indicated significant activity of T/C values ≥125 (page 467, Table I).

However, Das et al. do not teach or suggest which structural features are responsible for the enhanced activity, and Das et al. also teaches away from palladium compounds by teaching palladium compounds having a lower activity than the corresponding platinum compounds, e.g., PdL2, wherein R and R′=n-propyl. Therefore, Das et al. do not guide a person of ordinary skill in the art to the particular compounds recited in the claims or that such compounds would have a several fold higher cytotoxic activity than corresponding platinum compounds.

In addition, on page 466, left column, 2nd paragraph Das et al refer to Livingstone and Mihkelson (1970) who reported that dialkyldithiophosphate complexes lost their carcinostatic activity when ethyl was replaced by other alkyl groups:

> "when ethyl was replaced by other alkyl groups, the activity of the nickel and palladium chelates was virtually zero (T/C≈100), indicating that minor changes in the ligand markedly effect the activity"

Thus, Das et al. do not teach that palladium complexes are generally suitable as cytotoxic agents or that palladium complexes are "generally" better than platinum complexes.

Given that neither Watt et al, Amtmann et al. nor Das et al. teach or suggest the general structural features that are responsible for an enhanced cytotoxic activity and Das et al. teach that the replacement of an ethyl group by

another alkyl group can result in losing the activity, a person of ordinary skill in the art would not have had any reasonable expectation of success that the specific compounds recited in claim 1 as amended would exhibit a several fold higher cytotoxic activity than platinum compounds.

Therefore, the claims are not obvious in view of the combined teachings of Watt et al., Amtmann et al. and Das et al. and Applicants request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. 103(a) over Watt et al in view of Amtmann et al. and further in view of Das et al.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #104354.B270041).

Respectfully submitted,

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